

## Complete Summary

---

### GUIDELINE TITLE

The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society.

### BIBLIOGRAPHIC SOURCE(S)

Frohman EM, Goodin DS, Calabresi PA, Corboy JR, Coyle PK, Filippi M, Frank JA, Galetta SL, Grossman RI, Hawker K, Kachuck NJ, Levin MC, Phillips JT, Racke MK, Rivera VM, Stuart WH. The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2003 Sep 9;61(5):602-11. [47 references]  
[PubMed](#)

## COMPLETE SUMMARY CONTENT

SCOPE  
 METHODOLOGY - including Rating Scheme and Cost Analysis  
 RECOMMENDATIONS  
 EVIDENCE SUPPORTING THE RECOMMENDATIONS  
 BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
 QUALIFYING STATEMENTS  
 IMPLEMENTATION OF THE GUIDELINE  
 INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
 CATEGORIES  
 IDENTIFYING INFORMATION AND AVAILABILITY

## SCOPE

### DISEASE/CONDITION(S)

Multiple sclerosis

### GUIDELINE CATEGORY

Diagnosis  
 Education  
 Risk Assessment  
 Technology Assessment

### CLINICAL SPECIALTY

Family Practice  
Neurology  
Radiology

## INTENDED USERS

Physicians

## GUIDELINE OBJECTIVE(S)

- To consider the evidence that magnetic resonance imaging (MRI) can prospectively predict the future conversion to clinically definite multiple sclerosis (CDMS) in patients presenting with a syndrome consistent with inflammatory demyelination
- To consider the evidence for the use of baseline and follow-up magnetic resonance imaging in the diagnosis of patients with suspected multiple sclerosis

## TARGET POPULATION

- Patients with symptoms suggestive of multiple sclerosis (MS)
- Patients presenting with a syndrome consistent with inflammatory demyelination

## INTERVENTIONS AND PRACTICES CONSIDERED

Magnetic resonance imaging (MRI)

## MAJOR OUTCOMES CONSIDERED

Specificity, sensitivity, positive predictive value, and diagnostic accuracy of magnetic resonance imaging (MRI) in multiple sclerosis (MS)

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A search was undertaken using the following terms: clinically isolated syndromes, multiple sclerosis, and magnetic resonance imaging. Guideline developers used the Medline database from 1966 to 2003. In addition, the reference lists of the articles identified were also reviewed to identify articles not found by the computer search. They reviewed the abstracts of these articles and further limited their assessment to English language studies that were prospective and utilized a

well-defined gold standard for the development of clinically definite multiple sclerosis (CDMS).

#### Inclusion/Exclusion

The guideline developers only reviewed articles that studied at least 20 patients. There were 22 such studies identified. All of these articles considered the risk of developing clinically definite multiple sclerosis in patients with clinically isolated syndrome (CIS), based on the presence or absence of magnetic resonance imaging (MRI) lesions within the brain or spinal cord.

#### NUMBER OF SOURCE DOCUMENTS

46 articles were originally identified

22 studies met inclusion criteria

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

##### Rating of Diagnostic Article

Class I: Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. In addition, there must be adequate accounting for dropouts with numbers sufficiently low to have minimal potential for bias.

Class II: Evidence provided by a prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).

#### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

### Translation of Evidence to Recommendations

Level A rating requires at least one convincing Class I study or at least two consistent, convincing Class II studies.

Level B rating requires at least one convincing Class II study or at least three consistent Class III studies.

Level C rating requires at least two convincing and consistent Class III studies.

### Rating of Recommendation

A = established as useful/predictive or not useful/predictive for the given condition in the specified population.

B = probably useful/predictive or not useful/predictive for the given condition in the specified population.

C = possibly useful/predictive or not useful/predictive for the given condition in the specified population.

U = data inadequate or conflicting. Given current knowledge, test/predictor is unproven.

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

External Peer Review

Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines were reviewed for accuracy, quality, and thoroughness by the American Academy of Neurology (AAN) members, topic experts, and pertinent physician organizations.

Final guidelines were approved by the American Academy of Neurology Therapeutics and Technology Assessment Subcommittee on April 16, 2002, the American Academy of Neurology Practice Committee on April 2, 2003, and the American Academy of Neurology Board of Directors on June 22, 2003. They were published in *Neurology* 2003;61:602-611.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Definitions of the strength of the recommendations (A, B, C, U) and classification of the evidence (Class I through Class IV) are provided at the end of the "Major Recommendations" field.

#### Recommendations

1. Magnetic resonance imaging (MRI) changes seen in multiple sclerosis (MS) are known to be nonspecific (refer to Table 2, entitled "Diagnostic Consideration in Patients with Suspected MS and/or MRI White Matter Abnormalities" in the original guideline document). Therefore, the information derived from imaging investigations must always be considered in the context of the specific clinical situation presented by an individual patient. As a result, the following recommendations are predicated on the exclusion, at baseline, of appropriate alternative conditions that can mimic MS or can mimic the radiographic findings seen in MS.
2. On the basis of consistent Class I, II, and III evidence, in patients with clinically isolated syndrome (CIS), the finding of three or more white matter lesions on a T2-weighted MRI scan is a very sensitive predictor (>80%) of the subsequent development of clinically definite MS (CDMS) within the next 7 to 10 years (Type A recommendation). It is possible that the presence of even a smaller number of white matter lesions (e.g., one to three) may be equally predictive of future MS although this relationship requires better clarification.
3. The presence of two or more gadolinium (Gd)-enhancing lesions at baseline is highly predictive of the future development of clinically definite MS (Type B recommendation).
4. The appearance of new T2 lesions or new gadolinium enhancement 3 or more months after a clinically isolated demyelinating episode (and after a baseline MRI assessment) is highly predictive of the subsequent development of clinically definite MS in the near term (Type A recommendation).
5. The probability of making a diagnosis other than MS in patients with clinically isolated syndrome with any of the above MRI abnormalities is quite low, once alternative diagnoses that can mimic MS or can mimic the radiographic findings of MS have been excluded (Type A recommendation).
6. The MRI features helpful in the diagnosis of primary progressive MS (PPMS) cannot be determined from the existing evidence (Type U recommendation).

#### Definitions:

#### Rating of Recommendation

A = Established as useful/predictive or not useful/predictive for the given condition in the specified population.

B = Probably useful/predictive or not useful/predictive for the given condition in the specified population.

C = Possibly useful/predictive or not useful/predictive for the given condition in the specified population.

U = Data inadequate or conflicting. Given current knowledge, test/predictor is unproven

#### Rating of Diagnostic Article

Class I: Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. In addition, there must be adequate accounting for dropouts with numbers sufficiently low to have minimal potential for bias.

Class II: Evidence provided by a prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).

#### CLINICAL ALGORITHM(S)

None provided

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

- These guidelines may assist physicians in making appropriate clinical decisions regarding the clinical utility of magnetic resonance imaging (MRI) in suspected multiple sclerosis (MS).
- With MRI techniques, occult disease activity can be demonstrated in 50 to 80% of patients at the time of the first clinical presentation. Prospective studies have shown that the presence of such lesions predicts the future conversion to clinically definite MS (CDMS). Indeed, in a young to middle-aged adult with a clinically isolated syndrome (CIS), once alternative diagnoses are excluded at baseline, the finding of three or more white matter lesions on a T2-weighted MRI scan (especially if one of these lesions is located in the periventricular region) is a very sensitive predictor (>80%) of the subsequent development of clinically definite MS within the next 7 to 10 years. Moreover, the presence of two or more gadolinium (Gd)-enhancing lesions at baseline and the appearance of either new T2 lesions or new gadolinium enhancement on follow-up scans are also highly predictive of the subsequent development of clinically definite MS in the near term.

#### POTENTIAL HARMS

Not stated

### QUALIFYING STATEMENTS

#### QUALIFYING STATEMENTS

- The guideline developers acknowledge inherent limitations of the literature. Any study of the predictive validity of magnetic resonance imaging (MRI) is dependant upon the gold standard used to establish the diagnosis of multiple sclerosis (MS). Generally, this standard is the development of clinically definite MS (CDMS) by some criteria, after some period of follow-up. Nevertheless, in a disease like MS (where the development of clinically definite MS can be delayed by decades from the onset of clinical symptoms) such a design has serious limitations, especially when the follow-up is either too short or too variable. Most studies of the predictive validity of MRI in MS are confounded by this limitation.
- This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The American Academy of Neurology recognizes that specific patient-care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

### IMPLEMENTATION OF THE GUIDELINE

#### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## RELATED QUALITY TOOLS

- [American Academy of Neurology \(AAN\) Guideline Summary for Clinicians: The Utility of MRI in Suspected MS](#)
- [American Academy of Neurology \(AAN\) Guideline Summary for Patients and Their Families: Diagnosis of MS Using Magnetic Resonance Imaging \(MRI\)](#)

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Frohman EM, Goodin DS, Calabresi PA, Corboy JR, Coyle PK, Filippi M, Frank JA, Galetta SL, Grossman RI, Hawker K, Kachuck NJ, Levin MC, Phillips JT, Racke MK, Rivera VM, Stuart WH. The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2003 Sep 9;61(5):602-11. [47 references]  
[PubMed](#)

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2003 Sep 9

### GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society  
Child Neurology Society - Medical Specialty Society

### SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

## GUIDELINE COMMITTEE

Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology  
Practice Committee of the Child Neurology Society

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Members of the Therapeutics and Technology Assessment Subcommittee: Douglas S. Goodin, MD (chair); Carmel Armon, MD; Elliot M. Frohman, MD, PhD; Robert S. Goldman, MD; David Hammond, MD; Chung Y. Hsu, MD, PhD; Andres M. Kanner, MD; David S. Lefkowitz, MD; Isaac E. Silverman, MD; Michael A. Sloan, MD; Yuen T. So, MD, PhD; Edgar J. Kenton III, MD; Wendy Edlund, AAN Staff Liaison

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

## GUIDELINE STATUS

This is the current release of the guideline.

## GUIDELINE AVAILABILITY

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the [AAN Web site](#).

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- American Academy of Neurology (AAN) guideline summary for clinicians: the utility of MRI in suspected MS. St. Paul (MN): American Academy of Neurology, 2003 Sep. Electronic copies: Available from the [AAN Web site](#).
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Electronic copies: Available from the [American Academy of Neurology Web site](#).

## PATIENT RESOURCES

The following is available:

- AAN guideline summary for patients and their families: diagnosis of MS using magnetic resonance imaging (MRI). St. Paul (MN): American Academy of Neurology, 2003 Sep. Electronic copies: Available from the [American Academy of Neurology \(AAN\) Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC STATUS

This summary was completed by ECRI on February 12, 2004.

## COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is copyrighted by the American Academy of Neurology.

© 1998-2004 National Guideline Clearinghouse

Date Modified: 11/15/2004

FIRSTGOV

